PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P06299PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2004/000289	03.03.2004	31.03.2003
International Patent Classification (IPC) or both national classification and IPC		
A61M1/36		
Applicant		
RADI MEDICAL SYSTEMS AB et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☐ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.12.2004	15.12.2005
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/SE2004/000289

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-10 as published

Claims, Numbers

1-18 filed with telefax on 05.04.2005

Drawings, Sheets

1/4-4/4 as published

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-18

   because:

   ☒ the said international application, or the said claims Nos. 9-18 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-8 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

Claims 1 , 9 , 17 and 18 are independent .
Claim 9 is for a method.

The following documents cited in the International Search report will be referred to by means of the following appellation:
D1 : US-A-5 626 623
D2 : US-A-5 129 394
D3 : US-2002-133 198

III

Claims 17 and 18 are not examined PCT-Rule 67.1.vi
These claims correspond original claims 20 and 21.
The claims concern software for computers only.
See for instance claim 17 "... directly loadable into the ... memory"
Only software can be loaded into a memory , no hardware.

III .2

Claims 9 - 16 are not examined PCT-Rule 67.1.iv
The method includes surgery because a pressure sensor has to be implanted in the patient see claim 9 - a.
Furthermore the method includes a therapy because the best possible pacing of the patient is searched for see claim 11 :
"choosing ... an optimal implant setting" .

III .3

Claim 1 is unclear PCT-Article 6
A continuous curve has merely ONE maximum value.
This maximum may occur several times but calculating an "average" of such a maximum is mathematically wrong because there is only one.

For instance $y = \sin x$ in the interval zero to 720 degrees (4π)

has maximum one which occurs twice namely at x = 90 and 450 degrees.

Probably what the Applicant intended to define in claim 1 is similar to the following:
Sinus in the interval 135 to 180° has the maximum 0.7.
Sinus in the consecutive interval 360 to 450 has the maximum 1.0
The average of these two "local" maxima is (0.7 + 1.0) : 2 = 0.85
Yet this is not what claim 1 defines:
In claim 1 line 10 there is a NUMBER of measurement periods.
According to description page 6 line 17 such a period can be ten seconds.
According to P.6 L.20 a measurement SESSION can be 60 minutes and consists of several measurement PERIODS.
Within a measurement period in claim 1 there is merely ONE maximum (of dP / dt).
For the plurality of measurement periods in claim 1 there is a PLURALITY or SET of maxima and an average or median is calculated for this SET see claim 1 line 11:
"the predefined parameter is the average ... of the maximum value of the set"
Here is a minor grammatical error:
"maximum value" should be the plural: "maximum valueS"
because there are several measurement periods with each their maximum.

See also fig 1 : In step-100 a measurement period starts and in step-108 it is questioned whether a measurement session is performed ie. a collection of several measurement-periods.
Thus the predefined parameter in claim 1 is the average of dP / dt - max from several separate measurement periods.
Thus there is only ONE such average.
Of course it is theoretically possible to calculate an average of several other averages but this is not in claim 1 and not in the description : there are several measurement periods giving several maximum values giving ONE average.

Claim 1 line 13 : For each measurement period the pacemaker (= medical implant) has a different setting ie. a different manner of pacing :

"... measurement periods related to different ... medical implant settings" In the last lines of claim 1 and bottom of fig 1 ONE of these settings is selected (or selectable) as the best.

Yet the criterium for this selection of the best setting is unclear, claim 1 last line:
"... setting is identified ... where the average ... is maximal"

As explained above there is merely ONE average of several maxima from several measurement periods.
ONE average value does not form a curve but merely a point, whereby it is obscure to discuss a "maximum" for this average.
Example:
In claim 1 maybe there are five measurement-periods with five dP / dt maxima of, say, 2, 3, 8, 9 and 10 .
Each of these maxima corresponds an individual pacemaker-setting.
The average of 2, 3, 8, 9 and 10 is 6.4
Thus even if claim 1 last line is interpreted as using the pacemaker-setting for the measurement period which contains the average dP / dt - value of 6.4 then claim 1 remains ambiguous because dP / dt = 6.4 is a mathematical average which may not correspond any PHYSICAL value of dP / dt in the five intervals.
For example the dP / dt - values in the third time-interval (having max 8) may vary between 7.5 and 8, not containing 6.4.

By comparison with prior art claim 1 has been interpreted either so that the optimal pacemaker setting is the one used in:

- the time interval or measurement period having the dP / dt - values being CLOSEST to THE average of the dP / dt - maxima

OR used in

- the measurement period where the average of the dP / dt - values (all of them in that time-period, not only max) is the highest among all measurement periods.

The same ambiguity as in claim 1 is in fig 1 step 104:

average of ONE maximum.

→ →

III .4

Merely as a guide for the Applicant for formulating new claims in a national procedure the following is mentioned about available prior art :

The above interpretation of claim 1 is not inventive over D1:
From D1 it is known that the maximum values of dP / dt
(P pressure in a heart ventricle) are of special interest
for monitoring the efficiency of a pacemaker see D1 column 11 lines 10 - 25:
"processor 380 ... derive the dP / dt signal from the right ventricular ...
A peak detector ... determines dP / dt - peak ... employed in the algorithm
... for delivering the optimum AV delay"
AV see column 3 line 28
"AV delay interval of an AV synchronous pacing"
The rest of claim 1 of the invention are trivial calculations and choices of parameters at dP / dt - max for the skilled cardiologist in cooperation with a computer-programmer.

Thus in D1 fig 5 a pressure-sensor 160 is used for pressure P.
The first order time derivative dP / dt is determined by the computer in fig 5 see D1 column 3 line 44:
"deriving ... dP / dt from the measured RVP signal" and col.9 L.5 - 10.
RVP is pressure in the RIGHT ventricle , but the pressure-sensor 160 naturally also is adapted to measure in the LEFT ventricle since the anatomies and geometries are almost identical.
Thus whether P-measurements are made in left- or right ventricle relates to a METHOD of use , not to the constructional features of the device.
See also D2 where P-measurements in the left ventricle are suggested for controlling a pacemaker.

In D1 fig 7AB in step 722 a pressure value EPAD-test
(Estimated Pulmonary Artery Diastolic pressure , D1 col.3 L.47)
is determined as an average of a number X of measured EPAD-values.
A low EPAD value is considered optimal for heart stimulation
see col.14 first lines:
"an EPAD-min value ... indicating a hemodynamic improvement"

In step 724 fig 7B if a desired minimum pressure EPAD-min is reached
then this A-V stimulation interval of the pacemaker is selected as
the best AV-opt , otherwise in steps 730 > 710 a new AV-pacing delay
is selected and the averaging over X measurements is repeated.
The above EPAD-values are measured or derived from RVP where dP / dt
is maximum see fig 1 "RVP at dP / dt - max " and col.11 L.10 - 15 :
"A peak detector in digital controller 330 determines the dP / dt - peak
and employs it to ... sample the corresponding RVP ...
and derive the EPAD value"

Thus the computer and P-sensor in D1 fig 5 is fully capable of finding
all dP / dt - max in right (RVP) or left ventricular pressure.
Instead of averaging these dP / dt - max directly then a derived value EPAD
found at each dP / dt - max is averaged in step 722 and
a minimum EPAD found.
It is considered a normal design option for a programmer adviced by
a cardiologist that in this averaging-software-algorithm the dP / dt - maxima
could be inserted instead of EPAD values because fig 1 and col. 11 L.10 - 15
clearly state that the dP / dt - maxima and EPAD-mimima
always occur simultaneously.

III .5

Relevance of D3
Here the pacemakers computer can select between
two algorithms 510 and 524 fig 5 where one of them is
an algorithm finding dP / dt - max for the left ventricle

see D3 page 8 - 0056.

➜

III .6

original disclosure :
The Applicant has stated that claim 1 consists of original claims 1 and 8.
In original claim 1 a detail of the implant-setting was indicated (implant = pacemaker) namely that the pacemaker setting includes a certain first time difference , see last lines of original claim 1.
This detail is no more in claim 1 , yet it is considered an allowable amendment under PCT-Article 34.2.b because it is clear from the diagram in fig. 1 that the implant setting need not include this time difference.

*

Claims

1. Pressure measurement device (2) provided with a pressure sensor (6) adapted to perform pressure measurements in the left ventricle of a heart (8), the pressure sensor (6) is connected to a measurement unit (10) to receive pressure measurement values obtained from said sensor, and a processing means (12) adapted to determine a set of pressure values, and also a set of first order time derivative values determined from the set of pressure values, characterized in that said processing means also is adapted to calculate a value of a predefined parameter of the set of first order time derivative values during a number of measurement periods, the predefined parameter is the average or median value of the maximum value of the set of first order time derivative values, wherein the pressure measurements are adapted to be performed during measurement periods related to different predetermined medical implant settings in a medical implant (20) controlling the application of stimulation pulses at least in the left and right ventricles of the heart, and that an optimal implant device setting is identified as the setting where the average or median value is maximal.

2. Pressure measurement device according to claim 1, characterized in that said device includes a display means (14) for displaying, preferably in real-time, during a measurement period, curves representing the set of pressure values and the set of determined first order time derivative values.

3. Pressure measurement device according to claim 1, characterized in that said device comprises a pressure measurement guidewire (4) at which said pressure sensor is arranged.

4. Pressure measurement device according to claim 1, characterized in that the pressure measurement device is arranged in said medical implant being a heart stimulating device, e.g. a pacemaker, cardioverter or defibrillator, and that said pressure sensor is arranged at a heart electrode lead connected to said heart stimulating device.

5. Pressure measurement device according to claim 1, characterized in that said value of the predefined parameter is added to a

measurement session list of measurement periods.

6. Pressure measurement device according to claim 1, characterized in that the pressure measurement is repeated for other predefined implant device settings.

7. Pressure measurement device according to claim 1, characterized in that the implant device setting is adapted to be varied during a measurement session according to a predefined search pattern.

8. Pressure measurement device according to claim 2, characterized in that values of the predefined parameter are displayed in a three dimensional illustration.

9. Method for monitoring, determining by measurement and calculation and graphically displaying physiological variables related to blood pressure, comprising at least following steps:

a) detecting continuously during a measurement period left ventricular pressure of a heart (P_{LV}), derived from a guidewire-mounted pressure sensor;

b) transducing said pressure to a processable signal and delivering said processable signal to a processing means being able to process said processable signal;

c) receiving said processable signal;

d) calculating the first order time derivative (dP_{LV}/dt) of said left ventricular pressure by processing said signal;

e) forming and displaying a set of values representing the pressure (P_{LV}) and the first order time derivative of said pressure (dP_{LV}/dt);

f) calculating the value of a predefined parameter of said set of first order time derivative values during the measurement period, the predefined parameter is the average or median value of the maximum values of the first order time derivative values, wherein the pressure measurements are performed during measurement periods using predetermined medical implant settings in a medical implant (20) controlling the application of stimulation pulses at least in the left and right ventricles of the heart, and that the implant setting includes a first time difference $\Delta 1$ being the time between stimulations in the left and right ventricles, and

g) displaying said calculated value in a measurement session list that may include calculated values from other measurement periods.

10. Method according to claim 9, characterized in that in step f) only parts of the set of first order time derivative values that fulfil certain calculation criteria are included in calculating the value of the predefined parameter, wherein this results in that artefacts and disturbances are suppressed.

11. Method according to claim 9, characterized in that the method further comprises the step of choosing the implant setting from the measurement session list that fulfils an optimal implant setting criterion.

12. Method according to claim 11, characterized in that said optimal implant setting criterion is to choose the maximum amplitude of the average values.

13. Method according to claim 9, characterized in that the implant setting further includes a second time difference Δ2 being the time between stimulations in the right atrium and the right or left ventricle.

14. Method according to claim 9, characterized in that the implant device setting is varied according to a predefined search pattern..

15. Method according to claim 9, characterized in that a measurement period is less than 30 seconds and preferably 10 seconds.

16. Method according to claim 9, characterized in that a measurement session list that may include calculated values from measurement periods obtained during a measurement session of less than 60 minutes and preferably less than 30 minutes.

17. A computer program product directly loadable into the internal memory storage of a processing means within a control unit, comprising the software code means for performing the steps of any claims 9-16.

18. A computer program product that can be stored on a computer usable

medium, comprising readable program for causing a processing means in a control unit to control an execution of the steps of any of the claims 9-16.